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To: NCIC HPV@EPA

cc:

Subject: Environmental Defense comments on Methyl 4-Formylbenzoate (CAS# 1571-08-0)

----- Forwarded by Anh Nguyen/DC/USEPA/US on 11/25/2003 02:43 PM -----

Richard_Denison@environmentaldefense.org on 11/25/2003 02:23:59 PM



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Subject: Environmental Defense comments on Methyl 4-Formylbenzoate (CAS# 1571-08-0)

(Submitted via Internet 11/25/03 to oppt.ncic@epa.gov, hpv.chemrtk@epa.gov, boswell.karen@epa.gov, chem.rtk@epa.gov, MTC@mchsi.com, and tadams@therobertsgroup.net)

Environmental Defense appreciates this opportunity to submit comments on the robust summary/test plan for Methyl 4-Formylbenzoate (CAS# 1571-08-0).

The Eastman Chemical Company, in response to the HPV Challenge, has submitted a Robust Summary/Test Plan describing available data and testing needs for Methyl 4-formylbenzoate (MFB, CAS# 1571-08-0). Our review of the Robust Summaries/Test Plan indicates there are limited data addressing the fate and toxicity of MFB. This is not unexpected, as MFB is a chemical byproduct formed in the synthesis of dimethyl terephthalate and has limited use in industrial applications.

However, a great deal of data are provided for structurally related compounds. In some cases, these data are not relevant or excessive, resulting in an overly long submission. The requested SIDS elements could be more concisely and more accurately addressed if data only for compounds most closely related to MFB were presented and used to bridge data for MFB. For example, data available for the likely metabolic precursor of MFB, dimethyl terephthalate, and one of its likely two primary metabolites, terephthalic acid, are appropriately included and used for bridging. However, the extensive use of data for additional compounds, e.g. benzyl acetate, some of it going back to the 1940's and not technically acceptable under today's standards, only serves to unnecessarily complicate this submission.

That said, the available data for MFB, plus that modeled or bridged for structurally related compounds, indicate that MFB is relatively non-toxic and would not be expected to persist in the environment.

The Test Plan contains an extensive discussion of the hydrolysis and metabolism of MFB to yield terephthalic acid. However, it fails to mention that these reactions also yield methanol. If metabolism proceeds as proposed, almost twenty percent of the MFB molecule is transformed into methanol. Methanol toxicity is not seen in studies with rodents and most other laboratory species because they readily metabolize methanol and are thus resistant to its toxicity. Humans, however, are uniquely sensitive to intoxication by methanol. Estimates of the relative sensitivity of humans vs. rodents indicate that humans are as much as ten times more sensitive to

intoxication by methanol than are rodents (IPCS 1997). Thus, many scientists familiar with methanol and/or chemicals metabolized to methanol do not consider data developed using rodents to be appropriate to assess human health risks.

However, we do not recommend additional studies of MFB, given that only primates are considered appropriate animal models for human sensitivity to methanol toxicity. The Test Plan should point out the fact that, due to their greater sensitivity to methanol intoxication, humans are likely to be more sensitive to methanol-mediated MFB intoxication than laboratory animals.

Additional Comments:

1. It is stated that potential for release into the environment and possible sources of human exposure are minimal, but supporting information is not presented in any detail. Given the fact that MFB is produced in very significant amounts, the lack of information to describe its transport, disposal and/or recycling is a significant oversight that should be addressed, especially if a claim of low release and exposure is to be made.

2. Page 3. SIDS is referred to as Safety Information Data Set. This acronym stands for Screening Information Data Set.

3. When data on MFB are available to address the requested SIDS elements, additional data for structurally related compounds should not also be presented. It serves little purpose to present and discuss data bridged from numerous other compounds when actual data for MFB are available. For example, there is excessive use of data for benzaldehyde, given that it is not even the most representative chemical from which to bridge data for MFB.

4. In the first two studies summarized in Section 4.3 of the Robust Summary, under "Remarks" it should be clearly stated that the data cited are for terephthalic acid rather than MFB.

Reference:

IPCS IpoCS?Environmental Health Criteria 196. ? Methanol ISBN 92 401571969
ISSN 0250-863X. Geneva: WHO, 1997.

Thank you for this opportunity to comment.

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